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DARBY & DARBY
ANNE E ZITRON PH D
805 THIRD AVENUE
NEW YORK NY 10022

EXAMINER	
PARAS JR,P	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILED

Office Action Summary	Application No. 09/344,189	Applicant(s) ROGLER, CHARLES E.	
	Examiner Peter Paras, Jr.	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8-12, 15-21, 24-33, and 35-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a chimeric, immunetolerant mouse lacking mature B and T cells and having a degenerated liver parenchyma which is repopulated with transplanted xenogenic mammalian hepatocytes which can be infected with a compatible hepatitis virus wherein the mouse comprises a urokinase-type plasminogen activator (uPA), which causes the liver degeneration, and is homozygous for a recombination activation gene 2 (RAG-2) knockout, which causes the immunodeficiency, as well as methods of making and using the same mouse does not reasonably provide enablement for any and all chimeric immunetolerant mice having a degenerated liver and comprising xenogenic mammalian hepatocytes which can be infected with a compatible hepatitis virus, and methods of making and using the same chimeric, immunetolerant mice. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is directed to a method of making a chimeric mouse, comprising creating an immunetolerant mouse which has a degenerated liver, and transplanting xenogenic

hepatocytes, capable of being infected with a compatible mammalian hepatitis virus, to the parenchyma of the degenerated liver. Claim 2 is directed to the same method wherein the hepatocytes are infected with hepatitis virus prior to transplantation. Claim 3 is directed to the same method wherein the hepatocytes are infected with hepatitis virus following transplantation. Claim 4 is directed to the same method wherein xenogenic hepatocytes are human, chimpanzee, baboon, wooly monkey, ground squirrel, or woodchuck. Claim 5 is directed to the same method wherein the compatible mammalian hepatitis virus is either hepatitis A, hepatitis C, hepatitis D coinfected with hepadnavirus, hepatitis E, hepatitis F, or hepadnavirus. Claim 8 is directed to a chimeric mouse for hepatitis comprising an immunetolerant mouse having a degenerated liver parenchyma repopulated with transplanted xenogenic mammalian hepatocytes that can be infected with a compatible mammalian hepatitis virus. Claim 9 is directed to the same mouse wherein the xenogenic hepatocytes are infected prior to transplantation. Claim 10 is directed to the same mouse wherein the hepatocytes are infected following transplantation. Claim 11 is directed to the same mouse wherein the mammalian hepatocytes are human, chimpanzee, baboon, wooly monkey, ground squirrel, or woodchuck. Claim 12 is directed to the same mouse wherein the hepatitis virus is one of the same hepatitis viruses of claim 5. Claims 15-21 are directed to a method for screening a test compound for antiviral activity comprising administering the same test compound to the same mouse comprising xenogenic mammalian hepatocytes that are infected with a hepatitis virus and assaying the level of viral replication in the same mouse as compared to a control mouse wherein the hepatocytes

are infected before or after transplantation, the hepatocytes are the same as the hepatocytes of claim 11, and the hepatitis virus is the same as the hepatitis virus of claim 5. Claim 24 is directed the same method wherein the antiviral compound is a member selected from the group consisting of interferons, cytokines, interleukins, growth factors, hormones, nucleoside analogues, and antisense DNA/RNA. Claim 25 is directed to a method of screening a test compound for anticancer activity comprising the same steps as in claim 15 and assaying for development of hepatocellular carcinoma. Claim 26 is directed to the same method wherein the same mouse is compared to a control mouse. Claim 27 is directed to the same method wherein the chimeric mouse has precancerous or malignant hepatic tissue wherein the development of hepatocellular carcinomas is assayed by monitoring for the prevention of the development of cancerous tissue. Claim 28 is directed to comparing the mouse of claim 27 to a control mouse which has not been administered the test compound. Claims 29-31 are directed to the same method wherein the xenogenic hepatocytes are infected prior to or after the transplantation step. Claim 32 is directed to the same method wherein the hepatocytes are the same as the hepatocytes of claim 11. Claim 33 is directed to the same method wherein the hepatitis virus is the same as the hepatitis virus of claim 5. Claim 35 is directed to the same method wherein the hepatocyte is derived from a woodchuck and the hepatitis virus is woodchuck hepatitis virus. Claim 36 is directed to the same method wherein the anticancer compound is a member selected from the group consisting of interferons, cytokines, interleukins, growth factors, hormones, nucleoside analogues, and antisense DNA/RNA.

The specification discusses that the invention features a chimeric mouse liver system for mammalian hepatitis. See page 7, lines 30-35. The specification discusses that the invention features a chimeric, immunetolerant mouse with a degenerated liver comprising mammalian xenogenic hepatocytes, which can be infected with a compatible hepatitis virus, a uPA transgene (which causes liver degeneration), and a homozygous RAG-2 gene knockout (which causes immunodeficiency such that the mouse lacks mature B and T cells). See page 5. While the specification provides extensive teachings pertaining to the creation of a uPA/RAG2 mouse [which is created by breeding a uPA transgenic mouse with a RAG-2 knockout mouse] which has a degenerated liver and lacks mature B and T cells such that the uPA/RAG-2 mouse is a recipient for transplanted xenogenic mammalian hepatocytes and can be infected with a compatible hepatitis virus, the specification fails to provide any relevant teachings or specific guidance with regard to the generation of any immunetolerant mouse having a degenerated liver, in particular when such a mouse is a transplant recipient of xenogenic hepatocytes which can be infected with a compatible hepatitis virus (as is consistent with the discussion of the specification). Furthermore, the specification fails to even describe transplantation of xenogenic hepatocytes into any immunetolerant mouse [including those immunotolerant mice with normal livers], only that such a mouse would be useful as a liver model system for mammalian hepatitis (for drug screening, for example). Thus, as enablement requires the specification to teach how to make and use the claimed invention, the specification fails to enable the production of any immunetolerant mouse having a degenerated liver which can be transplanted with

xenogenic mammalian hepatocytes and infected with a compatible hepatitis virus such that the mouse may be used as a liver model system for mammalian hepatitis.

[**Note** that although the claimed chimeric mouse comprising a degenerated liver is not limited to receiving transplanted xenogenic hepatocytes, with regard to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enabled scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. As such, the broadest reasonable interpretation of the claimed chimeric uPA/RAG-2 mouse having a degenerated liver is one that can be a recipient of transplanted xenogenic mammalian hepatocytes such that the xenogenic hepatocytes are infected with a compatible mammalian hepatitis virus to produce a liver model system for mammalian hepatitis virus *(i.e.*, it is unknown what other purpose the chimeric mouse would serve if the xenogenic mammalian hepatocytes are not infected with a compatible mammalian hepatitis virus to produce a liver model system for mammalian hepatitis as is consistent with the teachings of the specification).]

With regard to claim breadth, it is unpredictable if any and all immunetolerant mice, other than a uPA/RAG-2 mouse, contain a degenerated liver such that xenogenic mammalian hepatocytes can be transplanted in the parenchyma of the degenerated liver. The specification fails to provide any guidance or relevant teachings which suggest that any and all immunetolerant mice contain degenerated livers. The

specification fails to provide working examples that correlate immunetolerance with liver degeneration. Actually, contrary to the claimed chimeric, immunetolerant (the term immunetolerant encompasses a nude mouse as well as an immunodeficient or SCID mouse as is consistent with the specification) mouse, a SCID mouse lacks mature B and T cells **but otherwise contains healthy organs** and appears to be normal. Kuby et al (1994,Immunology, 2nd edition, page 26) support this observation by suggesting that "apart from their lack of functional T and B cells, SCID mice appear to be normal in all respects" (see column 1, paragraph 3). The state of the art teaches that uPA transgenic mice contain degenerated livers resulted from expression of the uPA transgene and can be purchased from Jackson Laboratories. Therefore, to be consistent with the teachings of the specification, only uPA/RAG-2 mice [progeny of a breeding between uPA and RAG-2 -/- mice] contain degenerated livers and are immunodeficient such that uPA/RAG-2 mice make suitable recipients of transplanted xenogenic mammalian hepatocytes.

Therefore, in view of the lack of direction or guidance provided by the specification which teaches the production of any and all immunetolerant mice that contain degenerated livers which can be recipients of xenogenic mammalian hepatocytes, the absence of working examples for the demonstration or correlation of immunetolerance with liver degeneration, the unpredictable state of the art with respect to any and all immunetolerant mice containing degenerated livers, and the breadth of the claims drawn to any and all immunetolerant mice it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "capable of " in claims 1 and 8 is a relative term which renders the claim indefinite. The term "capable of" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not from the claim as written if the xenogenic mammalian hepatocytes are actually infected. For the claims to be consistent with the teachings of the specification the xenogenic mammalian hepatocytes must be infected with a compatible hepatitis virus such that the chimeric mouse can serve a liver system model for mammalian hepatitis virus.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-36 are rejected under 35 U.S.C. 102(a) as being anticipated by Petersen et al (ref 18, IDS).

Claim 1 is directed to a method of making a chimeric mouse, comprising creating an immunetolerant mouse which has a degenerated liver, and transplanting xenogenic hepatocytes, capable of being infected with a compatible mammalian hepatitis virus, to the parenchyma of the degenerated liver. Claim 2 is directed to the same method wherein the hepatocytes are infected with hepatitis virus prior to transplantation. Claim 3 is directed to the same method wherein the hepatocytes are infected with hepatitis virus following transplantation. Claim 4 is directed to the same method wherein xenogenic hepatocytes are human, chimpanzee, baboon, wooly monkey, ground squirrel, or woodchuck. Claim 5 is directed to the same method wherein the compatible mammalian hepatitis virus is either hepatitis A, hepatitis C, hepatitis D coinfected with hepadnavirus, hepatitis E, hepatitis F, or hepadnavirus. Claims 6-7 are directed to the same method wherein the mouse is a uPA/RAG-2 mouse, the hepatocytes are derived from a woodchuck, and the hepatitis virus is woodchuck hepatitis virus Claim 8 is directed to a chimeric mouse for hepatitis comprising an immunetolerant mouse having a degenerated liver parenchyma repopulated with transplanted xenogenic mammalian hepatocytes that can be infected with a compatible mammalian hepatitis virus. Claim 9 is directed to the same mouse wherein the xenogenic hepatocytes are infected prior to transplantation. Claim 10 is directed to the same mouse wherein the hepatocytes are infected following transplantation. Claim 11 is directed to the same mouse wherein the mammalian hepatocytes are human, chimpanzee, baboon, wooly monkey, ground squirrel, or woodchuck. Claim 12 is directed to the same mouse wherein the hepatitis virus is one of the same hepatitis viruses of claim 5. Claims 13-14 are directed to the

same mouse wherein the mouse is a uPA/RAG-2 mouse, the hepatocytes are derived from a woodchuck, and the hepatitis virus is woodchuck hepatitis virus. Claims 15-21 are directed to a method for screening a test compound for antiviral activity comprising administering the same test compound to the same mouse comprising xenogenic mammalian hepatocytes that are infected with a hepatitis virus and assaying the level of viral replication in the same mouse as compared to a control mouse wherein the hepatocytes are infected before or after transplantation, the hepatocytes are the same as the hepatocytes of claim 11, and the hepatitis virus is the same as the hepatitis virus of claim 5. Claims 22-23 are directed to the same method wherein the mouse is a uPA/RAG-2 mouse, the hepatocytes are derived from a woodchuck, and the hepatitis virus is woodchuck hepatitis virus. Claim 24 is directed the same method wherein the antiviral compound is a member selected from the group consisting of interferons, cytokines, interleukins, growth factors, hormones, nucleoside analogues, and antisense DNA/RNA. Claim 25 is directed to a method of screening a test compound for anticancer activity comprising the same steps as in claim 15 and assaying for development of hepatocellular carcinoma. Claim 26 is directed to the same method wherein the same mouse is compared to a control mouse. Claim 27 is directed to the same method wherein the chimeric mouse has precancerous or malignant hepatic tissue wherein the development of hepatocellular carcinomas is assayed by monitoring for the prevention of the development of cancerous tissue. Claim 28 is directed to comparing the mouse of claim 27 to a control mouse which has not been administered the test compound. Claims 29-31 are directed to the same method wherein the

xenogenic hepatocytes are infected prior to or after the transplantation step. Claim 32 is directed to the same method wherein the hepatocytes are the same as the hepatocytes of claim 11. Claim 33 is directed to the same method wherein the hepatitis virus is the same as the hepatitis virus of claim 5. Claim 34 is directed to the same method wherein the mouse is a uPA/RAG-2 mouse. Claim 35 is directed to the same method wherein the hepatocyte is derived from a woodchuck and the hepatitis virus is woodchuck hepatitis virus. Claim 36 is directed to the same method wherein the anticancer compound is a member selected from the group consisting of interferons, cytokines, interleukins, growth factors, hormones, nucleoside analogues, and antisense DNA/RNA.

Petersen et al teach a chimeric uPA/RAG-2 mouse (which is the offspring of a cross between a uPA mouse and a RAG-2 mouse, see page 311, methods: Generation of Tolerant uPA/RAG-2 mice) having a degenerated liver and containing woodchuck hepatocytes (see results first paragraph). Petersen et al teach that the woodchuck hepatocytes may be infected with woodchuck hepatitis virus (WHV, which is hepadnavirus) prior to (page 312 first paragraph, and page 314 first paragraph) or after transplantation (page 313 section: Infection of woodchuck hepatocytes in uPA/RAG-2 mice). Petersen et al tested the effects of interferon α and dexamethasone for antiviral (page 313) and anticancer (page 313, and discussion: whole text) activity in the same chimeric mice, as compared to controls, that were infected with woodchuck hepatitis virus prior to and/or after transplantation of woodchuck hepatocytes. Petersen et al teach the formation of hepatocellular carcinomas from transplanted premalignant tissue

as well as the presence of unique viral integration sites in a chimeric mouse as compared to a control donor mouse. Thus, the teachings of Petersen et al meet all of the instant claim limitations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

Claims 1-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rhim et al (ref 8, IDS) in view of Roggendorf (ref 9, IDS).

Claim 1 is directed to a method of making a chimeric mouse, comprising creating an immunetolerant mouse which has a degenerated liver, and transplanting xenogenic hepatocytes, capable of being infected with a compatible mammalian hepatitis virus, to the parenchyma of the degenerated liver. Claim 2 is directed to the same method wherein the hepatocytes are infected with hepatitis virus prior to transplantation. Claim 3 is directed to the same method wherein the hepatocytes are infected with hepatitis virus following transplantation. Claim 4 is directed to the same method wherein xenogenic hepatocytes are human, chimpanzee, baboon, wooly monkey, ground squirrel, or woodchuck. Claim 5 is directed to the same method wherein the compatible mammalian hepatitis virus is either hepatitis A, hepatitis C, hepatitis D coinfected with hepadnavirus, hepatitis E, hepatitis F, or hepadnavirus. Claims 6-7 are directed to the

same method wherein the mouse is a uPA/RAG-2 mouse, the hepatocytes are derived from a woodchuck, and the hepatitis virus is woodchuck hepatitis virus Claim 8 is directed to a chimeric mouse for hepatitis comprising an immunetolerant mouse having a degenerated liver parenchyma repopulated with transplanted xenogenic mammalian hepatocytes that can be infected with a compatible mammalian hepatitis virus. Claim 9 is directed to the same mouse wherein the xenogenic hepatocytes are infected prior to transplantation. Claim 10 is directed to the same mouse wherein the hepatocytes are infected following transplantation. Claim 11 is directed to the same mouse wherein the mammalian hepatocytes are human, chimpanzee, baboon, wooly monkey, ground squirrel, or woodchuck. Claim 12 is directed to the same mouse wherein the hepatitis virus is one of the same hepatitis viruses of claim 5. Claims 13-14 are directed to the same mouse wherein the mouse is a uPA/RAG-2 mouse, the hepatocytes are derived from a woodchuck, and the hepatitis virus is woodchuck hepatitis virus. Claims 15-21 are directed to a method for screening a test compound for antiviral activity comprising administering the same test compound to the same mouse comprising xenogenic mammalian hepatocytes that are infected with a hepatitis virus and assaying the level of viral replication in the same mouse as compared to a control mouse wherein the hepatocytes are infected before or after transplantation, the hepatocytes are the same as the hepatocytes of claim 11, and the hepatitis virus is the same as the hepatitis virus of claim 5. Claims 22-23 are directed to the same method wherein the mouse is a uPA/RAG-2 mouse, the hepatocytes are derived from a woodchuck, and the hepatitis virus is woodchuck hepatitis virus. Claim 24 is directed the same method wherein the

antiviral compound is a member selected from the group consisting of interferons, cytokines, interleukins, growth factors, hormones, nucleoside analogues, and antisense DNA/RNA. Claim 25 is directed to a method of screening a test compound for anticancer activity comprising the same steps as in claim 15 and assaying for development of hepatocellular carcinoma. Claim 26 is directed to the same method wherein the same mouse is compared to a control mouse. Claim 27 is directed to the same method wherein the chimeric mouse has precancerous or malignant hepatic tissue wherein the development of hepatocellular carcinomas is assayed by monitoring for the prevention of the development of cancerous tissue. Claim 28 is directed to comparing the mouse of claim 27 to a control mouse which has not been administered the test compound. Claims 29-31 are directed to the same method wherein the xenogenic hepatocytes are infected prior to or after the transplantation step. Claim 32 is directed to the same method wherein the hepatocytes are the same as the hepatocytes of claim 11. Claim 33 is directed to the same method wherein the hepatitis virus is the same as the hepatitis virus of claim 5. Claim 34 is directed to the same method wherein the mouse is a uPA/RAG-2 mouse. Claim 35 is directed to the same method wherein the hepatocyte is derived from a woodchuck and the hepatitis virus is woodchuck hepatitis virus. Claim 36 is directed to the same method wherein the anticancer compound is a member selected from the group consisting of interferons, cytokines, interleukins, growth factors, hormones, nucleoside analogues, and antisense DNA/RNA.

Rhim et al teach a chimeric mouse which comprises an albumin-urokinase transgene on an immunotolerant background (nude) having a degenerated liver and containing transplanted rat hepatocytes. Rhim et al discuss that such immunotolerant mice would support the growth of transplanted hepatocytes from other species and would be **valuable tools for studying liver biology of other species, including humans, in a controlled, *in vivo* experimental setting** (see page 4942, also materials and methods: Generation of Immunotolerant Alb-uPA transgenic mice). Rhim et al further discuss the possibility that **chimeric mice containing human hepatocytes could be used as a repository for human hepatocytes, as reagents for human carcinogenicity studies, or as models for human liver disease.**

Rhim et al differ from the claimed invention by not teaching: infection of the transplanted xenogenic hepatocytes with a compatible hepatitis virus, a method of screening of potential antiviral and anticancer compounds using the chimeric mouse of the claimed invention, and use of a SCID mouse as the donor of the immunotolerant component of the chimeric mouse.

However at the time the claimed invention was made, Roggendorf et al teach a woodchuck model for human hepatitis B virus infection. Roggendorf et al teach that the woodchuck hepatitis virus (WHV) closely resembles the human hepatitis B virus and is currently used in many laboratories to study pathogenesis of hepadnavirus infections, molecular mechanisms of hepatocellular carcinoma development, and cell tropism of hepadnaviruses. Woodchucks are also used to test vaccines to hepadnaviruses and evaluate antiviral drugs in chronic WHV infection (see introduction page 100, and pages

107-109, especially table 3 on page 109). Roggendorf et al generally throughout the whole document contrast woodchuck hepatitis virus with human hepatitis B virus and ground squirrel hepatitis virus.

Accordingly, in view of the teachings of Roggendorf et al, it would have been prima facie obvious for one of ordinary skill in the art to modify the teachings of Rhim et al by creating chimeric, immunotolerant mouse that contains transplanted woodchuck hepatocytes wherein the transplanted woodchuck hepatocytes can be infected with WHV such that the chimeric infected mouse may be used to screen for potential antiviral and anticancer compounds. It would have also been obvious to make a similar chimeric mouse using transplanted human hepatocytes to be used in the same methods as suggested by Rhim et al (see above bolded text). One of ordinary skill in the art would have been sufficiently motivated to make such modifications as it is an art recognized goal to develop treatment for human hepatitis and hepatocellular carcinomas as suggested by Rhim (see above bolded text).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at 703-305-6608. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is 703-308-0196.

Peter Paras, Jr.

Art Unit 1632